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### REMARKS

1. Status of the Claims

Claims 1-16, 19-32 and 39 are pending.

Claims 16, 22, 25, 26 and 28-30 stand allowed.

Claims 1-15, 19-21, 23, 24, 27, 31, 32 and 39 stand rejected.

Claims 1, 2, 16, 23 and 39 are amended herein.

Claims 19-21, 24, 27 and 31 are canceled by this amendment.

Reconsideration is respectfully requested.

2. Amendments to the Specification

The Applicants have noted several typographical errors and informalities, which Applicants have corrected in this Amendment. In the specification, clauses beginning on page 5, line 3 and on page 22, line 24 and paragraphs beginning on page 27, line 12, on page 30, line 6, on page 64, line 14, and on page 77, line 8 have been amended to correct minor editorial problems. The Applicants apologize for these errors.

3. Amendments to the Claims

Applicants have also noted some typographical errors and informalities in the claims which are corrected by this Amendment. In claim 1 under the definition of  $R^3(o)$  and claim 2 under clause (1), the first instance of "cycloalkylalkynyl" has been replaced by "cycloalkylalkenyl" to correct a typographical error. In claim 16, an extra ";" has been removed under the definition of  $R^3(f)$ . In claims 16 and 39, "heteroaryl selected from" has been removed under the definition of  $R^3(g)$  and "substituted phenyl selected from" has been removed under the definition of  $R^3(h)$  because these elements are not presented in formal Markush format.

4. Claim Election/Restrictions

The Examiner noted that newly submitted claim 39 (in-part) was directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

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the invention which has been examined is where A and B are "simultaneously" an aryl or heteroaryl ring. Newly added claim 39 claims that A and B "each independently" is an aryl or heteroaryl ring. Since the Applicants received an action on the merits for the originally presented invention, this invention was constructively elected by original presentation for prosecution on the merits. Accordingly, the Examiner withdrew claim 39 (in-part) from consideration as being directed to non-elected inventions.

The Applicants have amended claim 39 to omit non-elected subject matter. Accordingly, the Applicants believe that claim 39 as presently amended meets the requirements of 37 CFR 1.142(b) and MPEP § 821.03.

5. Rejections Under 35 USC § 112, Second Paragraph

The Examiner rejected claims 1-15, 19-21, 23, 24, 27, 31, 32 and 39 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention.

a. "Or"

The Examiner pointed out that in claim 1, under the definition of  $R^3(r)$  an "or" is needed before "-OC(O)-NR'R'". Claim 1 has been amended to make this correction.

b. Lack of Antecedent Basis for  $R^6$

The Examiner pointed out that in claims 19-21, 24, 27 and 31, the  $R^6$  variable lacks antecedent basis from the claims from which they depend. Claims 19-21, 24, 27 and 31 have been canceled.

c. Lack of Antecedent Basis for First Four Substituents

The Examiner pointed out that in claim 23, the first four (4) substituents lack antecedent basis from claim 22. The Applicants have amended claim 23 to remove the substituents noted by the Examiner.

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d. "Heteroalkyl"

The Examiner pointed out that in claim 39, under the definition of  $R^3$ (f), "heteroalkyl" is misspelled. Claim 39 has been amended to make this correction.

e. Period

The Examiner pointed out that claim 39 does not conform to M.P.E.P. 608.01(m) since each claim must end with a period and no other periods may be used elsewhere in the claims except for abbreviations {e.g., see the period before the definition of  $R^4$ }. The Applicants have amended claim 39 to remove redundant language and the extra period, which reappear at the end of the claim, to recite, *inter alia*,

(h) ~~substituted phenyl selected from~~ sulfamoylphenyl,  
methylsulfonylphenyl, carboxyphenyl or ethoxycarbonylphenyl; ~~and~~  
~~prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts~~  
~~thereof.~~

The Applicants believe, in view of the amendments noted above, that all of the Applicants' presently pending claims meet the criteria of 35 USC § 112, second paragraph.

6. Rejections Under 35 USC §103

The Examiner rejected claims 1-7, 12 and 32 under 35 USC §103(a) as being unpatentable over Faraci et al., WO 94/13643 (US 5712303). The Examiner re-iterated previous bases for rejection, stating, *inter alia*, that the difference between the teachings of Faraci et al. and Applicants' invention was that of generic description of the products being administered for the intended use.

The Applicants understand that the 103(a) rejection is based on the rationale that certain selections for  $R^3$  in claim 1 overlap with selections for the substituents on the ring  $R^3$  in Faraci (for example, see the products on page 36, line 10; page 40, line 15; page 43, line 19; and page

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44 lines 12-14). The Applicants have amended claim 39 to remove the overlap noted by the Examiner. In particular, claim 1 as amended recites that  $R^3$  may be selected from:

- (a) optionally substituted heterocyclyl;
- (b) ~~optionally substituted aryl or heteraryl;~~
- (c) heteroalkenyl;
- (d) heteroalkynyl;
- (e) optionally substituted heterocyclylalkyl;
- (f) optionally substituted heterocyclylalkenyl;
- (g) optionally substituted heterocyclylalkynyl;
- (h) optionally substituted heterocyclylalkoxy, cycloxy or heterocycloxy;
- (i) optionally substituted heterocyclylalkylamino;
- (j) optionally substituted heterocyclylalkylcarbonyl;
- (k)  $-Y-(alkylene)-R^9$  where:  
Y is a single bond,  $-O-$ ,  $-NH-$  or  $-S(O)_n-$  (where n is an integer from 0 to 2); and  
 $R^9$  is cyano, optionally substituted heteroaryl,  $-COOH$ ,  $-COR^{10}$ ,  $||-||COOR^{11}$ ,  $-CONR^{12}R^{13}$ ,  $-SO_2R^{14}$ ,  $-SO_2NR^{15}R^{16}$ ,  $-NHSO_2R^{17}$  or  $-NHSO_2NR^{18}R^{19}$ , where  $R^{10}$  is optionally substituted heterocycle,  ~~$R^{11}$  is alkyl~~, and  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$  and  $R^{19}$  are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (l)  $-C(=NR^{20})(NR^{21}R^{22})$  where  $R^{20}$ ,  $R^{21}$  and  $R^{22}$  independently represent hydrogen, alkyl or hydroxy, or  $R^{20}$  and  $R^{21}$  together are  $-(CH_2)_n-$  where n is 2 or 3 and  $R^{22}$  is hydrogen or alkyl;
- (m)  $-NHC(X)NR^{23}R^{24}$  where X is  $-O-$  or  $-S-$ , and  $R^{23}$  and  $R^{24}$  are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (n)  $-CONR^{25}R^{26}$  where  $R^{25}$  and  $R^{26}$  independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or

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R<sup>25</sup> and R<sup>26</sup> together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

- (o) cycloalkylalkyl, ~~cycloalkylalkynyl~~ cycloalkylalkenyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (p) arylaminoalkylene or heteroarylaminoalkylene;
- (q) Z-alkylene-NR<sup>30</sup>R<sup>31</sup> or Z-alkylene-OR<sup>32</sup> where Z is -O-, and R<sup>30</sup>, R<sup>31</sup> and R<sup>32</sup> are independently of each other, hydrogen, alkyl or heteroalkyl;
- (r) -OC(O)-alkylene-CO<sub>2</sub>H [i.e.] or -OC(O)-NR'R'' (where R' and R'' are independently hydrogen or alkyl);
- (s) heteroarylalkenylene or heteroarylalkynylene; and
- (t) heteroalkylamino;

Element (b) has been removed and element (k) has been amended to remove "-COOR<sup>11</sup>" to remove overlap between selections for R<sup>3</sup> in claim 1 and selections for the substituents on the ring R<sup>3</sup> in Faraci noted by the Examiner (for example, see the products on page 36, line 10; page 40, line 15; page 43, line 19; and page 44 lines 12-14). Element (o) has been amended such that the first instance of "cycloalkylalkynyl" has been replaced by "cycloalkylalkenyl" due to a typographical error as discussed above. Clause (r) has been amended to include an "or" to conform to the requirements of 35 USC § 112, second paragraph, discussed above.

Therefore, Applicants' invention as now claimed in amended claim 1 is not disclosed or suggested by Faraci. Applicants' invention is further nonobvious in light of the unexpected and surprising p38 activity, which is neither taught nor suggested by Faraci. Accordingly, the Applicants believe, in view of the amendments noted above, that claims 1-7, 12 and 32 meet the criteria of 35 USC §103 as patentable over Faraci, and Applicants respectfully request that this rejection be withdrawn.

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**FEES**

No fees should be due. However, in the event it is determined that a fee is due,  
please charge same to Deposit Account No. 18-1700.

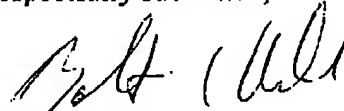
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-852-1141.

Respectfully submitted,



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